

## **Multidisciplinary Rehabilitation Programs for Moderate to Severe Traumatic Brain Injury in Adults: Future Research Needs**

**Identification of Future Research Needs From Comparative Effectiveness Review No. 72**

**Prepared for:**

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The information in this report is intended to help health care researchers and funders of research make well-informed decisions in designing and funding research and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of scientific judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical research and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances.

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limited the ability to answer the systematic review questions. AHRQ supports EPCs to work with various stakeholders to identify and prioritize the future research that are needed by decisionmakers. This information is provided for researchers and funders of research in these Future Research Needs papers. These papers are made available for public comment and use and may be revised.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The evidence reports undergo public comment prior to their release as a final report.

We welcome comments on this Future Research Needs document. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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# Executive Summary

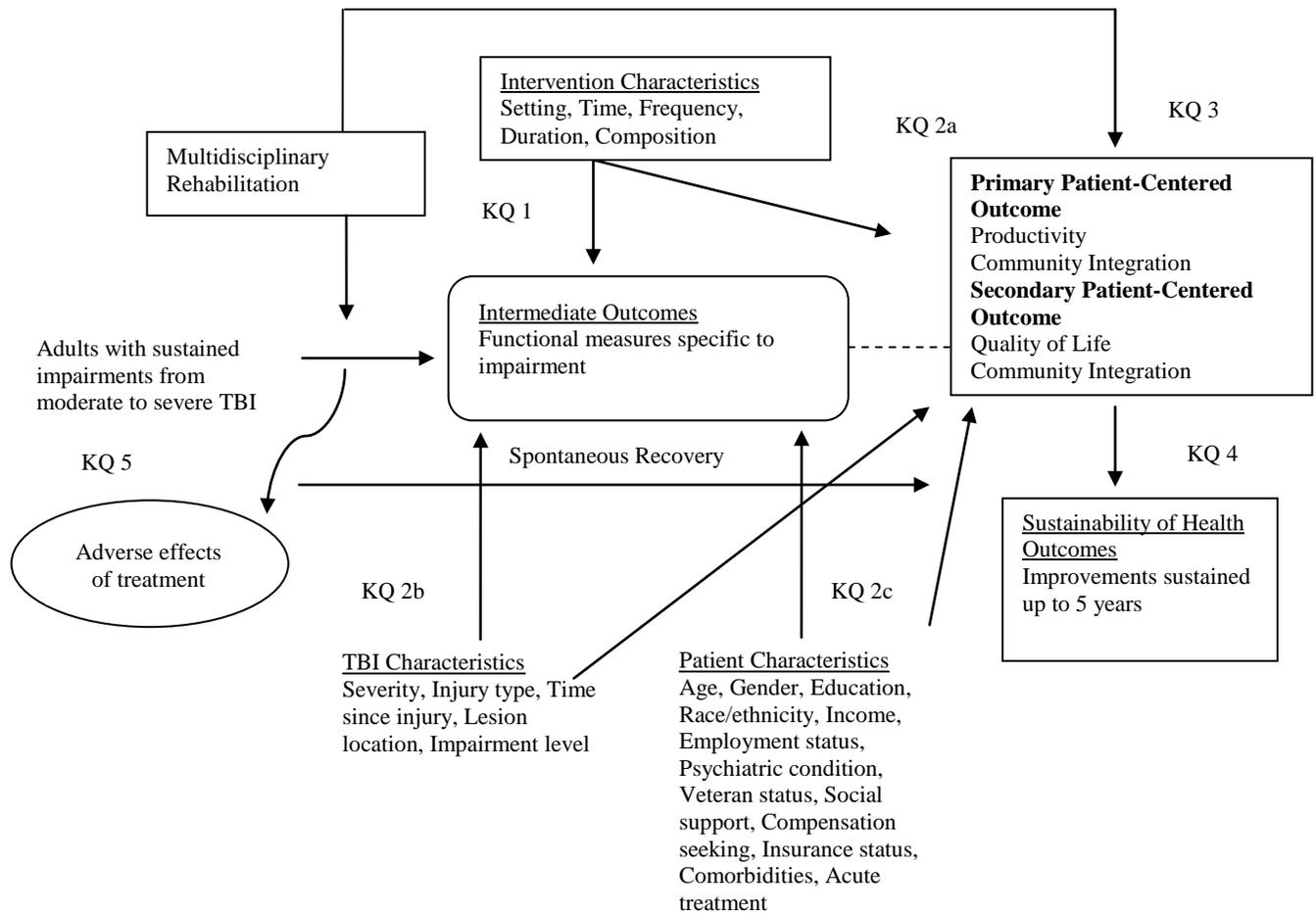
## Background

This Future Research Needs (FRN) project is a followup to the recently completed Comparative Effectiveness Review (CER) “Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults.”<sup>1</sup> The CER was motivated by uncertainty around the effectiveness and comparative effectiveness of rehabilitation programs for adult patients with sustained impairments from moderate to severe traumatic brain injury (TBI). This FRN project aims to identify and prioritize specific gaps in the current literature about the effectiveness and comparative effectiveness of multidisciplinary rehabilitation programs for which additional research would aid decisionmakers.

We used a deliberative process to identify evidence gaps, translate gaps into researchable questions, and solicit stakeholder opinion on the importance of research questions. This report proposes specific research needs along with research design considerations that may help advance research in this field.

We adapted the analytic framework from the original draft CER (Figure A). The framework describes a process experienced by adults with sustained impairments from a moderate to severe TBI entering multidisciplinary rehabilitation programs. The review addressed important Key Questions (KQs) about how these programs are characterized (KQ 1); evaluating the evidence about the comparative effectiveness of these programs in regard to participation (KQ 2); the identification and use of minimal clinically important differences (MCIDs) for key outcomes instruments (KQ 3); the sustainability of the improvements made during rehabilitation (KQ 4); and potential harms of multidisciplinary rehabilitation programs (KQ 5).<sup>1</sup>

**Figure A. Analytic framework**



KQ = Key Question; TBI = traumatic brain injury

The literature search conducted for the CER covered material indexed through January 2012. Our intent was to identify and synthesize data from relevant comparative effectiveness research on multidisciplinary rehabilitation programs to inform treatment decisions. The primary outcome of interest was participation in community life as indicated by productivity or select measures of community integration.

For KQ 1, we found that multidisciplinary postacute rehabilitation programs for impairments from moderate to severe TBI varied widely in terms of populations targeted, setting, program intensity and duration, and timing of intervention. Clear categorization of all studied interventions was not possible. However, the most frequently studied programs are those based upon the comprehensive holistic day treatment model of care. These programs maintained a similar approach and mode of delivery. Individuals were enrolled in and progressed through structured intensive day-treatment programs in small groups of individuals that received several hours of treatments per day, several days per week. Treatment was delivered largely through group sessions, while maintaining an emphasis on addressing individual needs. Emphases included self-awareness of impairments and compensatory approaches to retraining, with vocational rehabilitation another key element.

From the evidence synthesized for KQ 2, we were unable to draw broad conclusions about effectiveness or comparative effectiveness of multidisciplinary rehabilitation programs. We found that a Comparative Effectiveness Review on such complex interventions led to conclusions about the very specific populations and interventions studied:

- We found insufficient evidence assessing effectiveness for productivity or community integration.
- We found low-strength evidence that gainful employment or return to military fitness did not differ significantly at 1-year posttreatment between an 6-week inpatient hospital treatment and a 8-week limited home-based treatment. Participants were active duty military patients with closed head injuries and with relatively mild impairment levels who were treated within 3 months of injury.
- We found low-strength evidence that productivity did not differ significantly at 1 year posttreatment between closed head injury participants of functional-experiential programs and cognitive-didactic inpatient rehabilitation programs. Both programs lasted an average of just over 1 month and were delivered in Veterans Affairs rehabilitation facilities. Participants began treatment within 6 months of injury.
- We found low-strength evidence that moderate to severe TBI survivors with chronic impairments judged to need 16 weeks of intensive treatment and who were enrolled in an integrated cognitive rehabilitation program achieved higher rates of return to community-based employment, but not higher rates of community integration, than participants of standard rehabilitation immediately posttreatment.
  - We found low-strength evidence that rates of return to community-based employment between the two groups equalized by 6 months posttreatment (rates in the standard rehabilitation group caught up with those of the integrated cognitive rehabilitation program group).

For KQ 3, we identified no evidence establishing an MCID for the Mayo-Portland Adaptability Inventory, the outcomes instrument of most interest to us. Although we identified some evidence that established and used an MCID with the Community Integration Questionnaire, overall we observed a limited use of MCIDs in available research.

We found very few eligible studies that conducted followup assessments to determine maintenance of rehabilitation gains as addressed by KQ 4. Two studies that evaluated followup outcomes yielded highly specific conclusions:

- We found low-strength evidence that improvements in return to community-based employment and Community Integration Questionnaire scores were sustained at 6 months posttreatment.
- We found low-strength of evidence that rates of participation in competitive work achieved at 6 months posttreatment appear to be sustained at 12 months posttreatment.

Lastly, few studies on this topic addressed KQ 5, adverse effects. One study that assessed adverse effects reported that none were observed.

The evidence we reviewed emphasized the complexity of traumatic brain injuries and the interventions to rehabilitate individuals suffering from associated sustained impairments. Our review, like others, found the currently available evidence about the effectiveness and comparative effectiveness of multidisciplinary rehabilitation programs for moderate to severe TBI in adults are limited. Specifically, we found insufficient evidence to assess efficacy or effectiveness, and identified few well-designed studies to address comparative effectiveness. Applicability of those studies also appears problematic. However, our CER findings should not

be misunderstood to be evidence of ineffectiveness. Rather, the findings provide justification for additional research in order to further establish understanding of these complex interventions.

To guide the development of additional comparative effectiveness research on this topic, this FRN project aims to identify specific evidence gaps and prioritize FRNs with research design considerations likely to advance the field.

## Methods

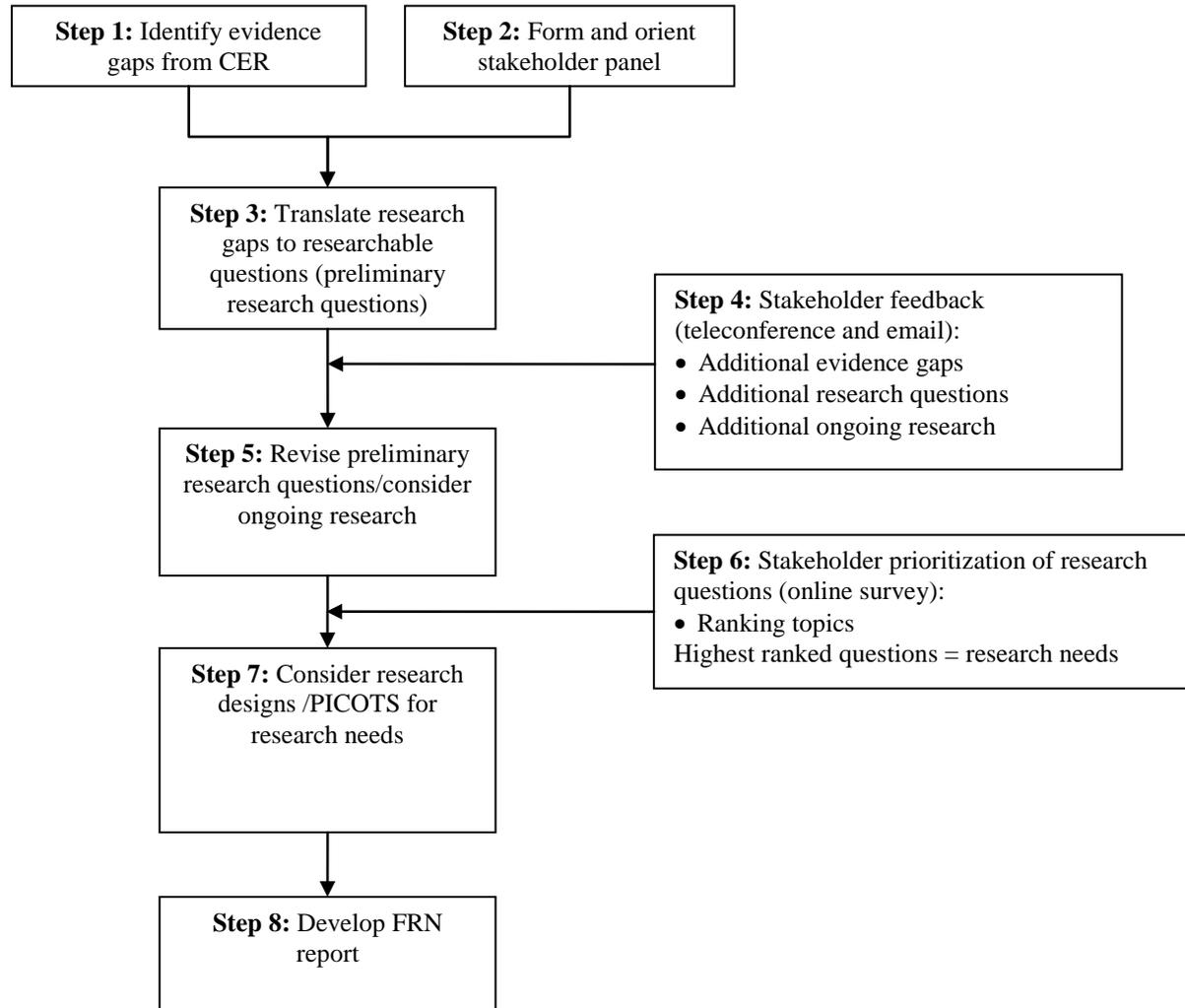
We used a deliberative process to identify and prioritize research questions relevant to the KQs addressed in the CER.<sup>1</sup> Figure B illustrates the eight steps used to accomplish the objectives of this project.

First, we translated the research gaps identified in the CER into research questions. Second, we assembled a diverse stakeholder panel with representation from various perspectives relevant to the topic. Invited research representatives were national experts who were familiar with: (1) evidence-based medicine; (2) the obstacles often associated with conducting well-designed research on this complex condition; and (3) interventions from the fields of physical medicine and rehabilitation, neuropsychology, and speech-language pathology. We invited participation from representatives from organizations supporting or conducting relevant research, including the U.S. Department of Veterans Affairs, U.S. Department of Defense, National Institute on Disability and Rehabilitation Research, National Institute of Neurological Disorders and Stroke, the American Academy of Physical Medicine and Rehabilitation, and the American Congress of Rehabilitation Medicine. We also invited policy and payer representation from the Centers for Medicare and Medicaid Services. Finally, we engaged providers and consumers, because the decisional dilemmas faced by these groups are critical to identifying and prioritizing research questions.

We first held conference calls with stakeholders to refine the draft research questions. Based upon these conversations and an assessment of recent and ongoing work, we revised our initial list of research questions. This revision included separating the questions into categories (methodological research questions that need to be addressed to enhance the usefulness of current effectiveness research, and topical research questions that have not been sufficiently addressed in the current literature). We sent this list of research questions to stakeholders for ranking. Stakeholders numerically ranked their top three methodological research questions from a total of seven and their top three topical research questions from a total of six.

Rankings were weighted based upon stakeholder numerical ordering of questions. Based upon natural breakpoints in the weighted rankings, we determined high-, moderate-, and low-priority research questions. High priority questions were deemed research needs. We then identified and discussed research design considerations for those identified research needs.

**Figure B. Project flow**



CER = Comparative Effectiveness Review; FRN = Future Research Needs; PICOTS = population, intervention, comparison, outcome, timing, setting.

## Results

### Prioritization Results

We analyzed weighted rankings for stakeholders participating in the Web-based prioritization process. Of the 10 stakeholders invited to rank research questions, 5 ranked methodological questions and 4 ranked topical questions.

### Methodological Research Needs

A natural breakpoint in weighted rankings revealed two methodological research needs. Addressing methodological research needs will enhance the utility and translation of current and future research on multidisciplinary rehabilitation programs for sustained impairments from moderate to severe TBI in adults:

- What outcomes of multidisciplinary rehabilitation are most important to:
  - Patients
  - Families
  - Payers
- Which patient characteristics confound/modify effectiveness of rehabilitation programs?

Methodological research needs pertain to identifying outcomes that are important to patients, families, and payers, and to identifying patient characteristics that influence response to rehabilitation.

## Considerations for Potential Research Designs

There are several ways that these methodological research needs could be addressed. Systematic reviews, epidemiological studies, and/or qualitative research would all assist in improving the understanding with regard to valued outcomes and factors that confound or modify the effect of TBI rehabilitation. One way to identify specific outcomes valued by patients may be to review the literature or secondary databases about TBI rehabilitation programs that use shared decisionmaking or goal setting among patients, families, and providers. Qualitative research would also be useful. Focus groups, for example, with representatives of patients, families, and payers – in separate focus groups- would help to identify these outcomes. Several patient and family focus groups would be necessary due to the wide range of impairment types and levels resulting from moderate to severe TBI. Preferred outcomes are likely associated with patient impairment types and levels at rehabilitation initiation.

Patient characteristics associated with the effectiveness of rehabilitation programs could be identified through similar methods. This process would benefit first from a systematic literature review. Several studies that examine patient characteristics and their influence on outcomes are available. A systematic review is not likely to provide the complete picture of confounding and effect modifying factors. Analysis of secondary databases and post hoc analysis of effectiveness studies establishing potential relationships between patient characteristics and patient outcomes should be included in such a systematic review. By definition, multidisciplinary rehabilitation programs involve several provider types; therefore a multidisciplinary approach to consensus development is essential. Participants should include clinical experts and researchers with expertise in clinical outcomes, epidemiology, biostatistics, and health services research.

## Topical Research Needs

Topical research needs primarily addressed the PICOTS (population, intervention, comparison, outcome, timing, and setting) elements of interventions, outcomes, and timing; a breakpoint in weighted rankings revealed three prominent topical research needs. Addressing these issues will enhance understanding of efficacy and comparative effectiveness, which was limited in the draft CER.

### First Topical Research Need

- Which multidisciplinary rehabilitation programs are “**promising practices?**”
- What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?
- What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?

- Which patients (**subgroups**) appear to benefit most by various multidisciplinary rehabilitation programs?
- What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?

### **Considerations for Potential Research Designs**

The draft CER and peer review of that draft emphasized the limited value of rigorous Comparative Effectiveness Reviews on this topic given the complexity of rehabilitation programs for TBI impairments and the current status of this literature. As topics for Comparative Effectiveness Reviews have expanded beyond pharmaceutical interventions, alternative approaches have been proposed to synthesize research on complex interventions (characterized as programs in which effects are dependent on context and implementation). These methods may be an option better suited to such topics. These reviews are rigorous systematic reviews, but focus more on explaining how, when, and why certain interventions may work or not work. This approach to a systematic review provides improved understanding of interventions and their populations and therefore may be a good fit for complex interventions such as rehabilitation.

### **Second Topical Research Need**

- **Timing:** At what stage of recovery do multidisciplinary rehabilitation programs offer patients the best chance of improvement?

Understanding the timing of enrollment in rehabilitation programs likely to maximize benefits received from rehabilitation is another research need. This question was addressed by the CER KQs. However, data was too limited assess the influence of rehabilitation program timing. This is especially critical in an environment of limited resources, because payers want to support rehabilitation when it can be most beneficial.

### **Considerations for Potential Research Designs**

A definitive test of the relationship between rehabilitation timing (in terms of functional status and/or time-since-injury) and outcomes could be attained through experimental studies. RCTs should provide the most valid results. However, given the heterogeneity in this population requiring restrictive inclusion/exclusion criteria, results would have limited generalizability. Additionally, the limited feasibility and ethical concerns of conducting RCTs in this population suggest that prospective cohort studies might best address this research question. These studies should be carefully conducted by measuring all potentially confounding variables necessary to statically adjust for selection bias and be designed with adequate power.

### **Third Topical Research Need**

- **Sustainability and followup:** Are benefits received from multidisciplinary rehabilitation programs sustained over the long term?
- What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods postrehabilitation?

The last identified research need also relates to timing. Our stakeholders were very concerned about improving evidence assessing whether and how TBI patients can maintain the gains made in rehabilitation. The CER addressed this question and found some evidence that rehabilitation gains were sustained in the few studies that included longer term followup. However, the strength of this evidence was low, timeframes rarely went beyond 1 year and study results may

have limited applicability. Stakeholders suggested that followup care is beneficial to maintaining rehabilitation gains, but little is known about how and why these benefits are conferred. None of the rehabilitation programs we examined for the CER had formal followup rehabilitation components. Additional research to examine the benefits of followup rehabilitation sessions would inform decisionmaking.

### **Considerations for Potential Research Designs**

Considerations similar to those mentioned in regard to topical research need number 2 would assist investigators in designing studies to test the hypothesized relationship of rehabilitation on long-term outcomes and followup rehabilitation on patient outcomes.

## **Discussion**

This FRN project refined and prioritized research needs relevant to the KQs addressed in the draft CER, “Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults.”<sup>1</sup> We conducted a deliberative process to refine and expand research gaps identified in the CER through conversations with stakeholders who represented various perspectives and expertise on the topic. This process identified seven methodological and six topical research questions thought to address identified evidence gaps. We then asked stakeholders to rank research questions according to their potential impact. The highly ranked questions were deemed research needs. Results from the ranking process revealed two methodological and three topical research needs.

Addressing methodological research needs will enhance the utility and comparability of future studies of multidisciplinary rehabilitation for moderate to severe TBI. These needs involve identifying patient centered outcomes and patient characteristics associated with response to rehabilitation.

Identified topical research needs demonstrate the importance of an enhanced understanding of (1) how and why multidisciplinary rehabilitation programs benefit specific types of patients and (2) the timing of rehabilitation that may be most beneficial and how to maintain or prevent deterioration after rehabilitation. Future studies of multidisciplinary rehabilitation programs should be designed to pay close attention to reducing bias as much as possible for the selected research design. Studies should be adequately powered to test hypothesized relationships, including among subgroups.

While a strength of this project is the intended variety of perspectives brought by broad stakeholder participation, we were not able to collect a representative perspective from a larger sample of stakeholders and had a low response rate to our stakeholder invitations and ranking process. This is a major limitation. The stakeholders participating in this project represented various perspectives on multidisciplinary rehabilitation programs for TBI. However, the prioritized research needs reflect the opinions of these stakeholders and may not be applicable to the broader population of stakeholders on this topic. This CER and related FRN project overlapped with several other projects tapping the same group of stakeholders and could explain the limited availability and interest in participation. Stakeholder discussions emphasized the need for federal agencies to work together to understand activities within each agency surrounding this topic.

## Conclusions

This FRN project identified several research needs thought relevant by a select group of stakeholders to move the field forward. The first research need was not directly addressed in our CER and therefore may need a systematic review to determine more specifically what these research gaps are:

- What outcomes of multidisciplinary rehabilitation are most important to:
  - Patients
  - Families
  - Payers

Remaining research needs were questions that would have been covered in the original CER, but evidence was insufficient and/or conclusions had limited applicability:

- Which patient characteristics confound/modify effectiveness of rehabilitation programs?
- Which multidisciplinary rehabilitation programs are “**promising practices?**”
  - What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?
  - What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?
  - Which patients (**subgroups**) appear to benefit most by various multidisciplinary rehabilitation programs?
  - What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?
- **Timing:** At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?
- **Sustainability and Followup:** Are benefits received from multidisciplinary rehabilitation programs sustained over the long term?
  - What level and type of followup care allows for maintenance of or prevents deterioration of rehabilitation gains at given time periods postrehabilitation?

## References

1. Brasure M, Lamberty GJ, Sayer NA, et al. Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults. Comparative Effectiveness Review No. 72. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2007-10064-I.) AHRQ Publication No. 12-EHC101-EF. Rockville, MD: Agency for Healthcare Research and Quality. June 2012.  
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# Background

## Context

This Future Research Needs (FRN) project is a followup to the recently completed Comparative Effectiveness Review (CER) “Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults.”<sup>1</sup> The CER was motivated by uncertainty around the effectiveness and comparative effectiveness of rehabilitation programs for adult patients with sustained impairments from moderate to severe traumatic brain injury (TBI). This FRN project aims to identify and prioritize specific gaps in the current literature about the effectiveness and comparative effectiveness of multidisciplinary rehabilitation programs for which additional research would aid decisionmakers. We used a deliberative process to identify evidence gaps, translate gaps into researchable questions, and solicit stakeholder opinion on the importance of research questions. This report proposes specific research needs along with research design considerations that could advance research in this field.

Our FRNs project identifies research needs within the scope of the CER. We used an analytical framework (Figure 1) to construct the following Key Questions (KQs):

**KQ 1:** How have studies characterized multidisciplinary postacute rehabilitation for TBI in adults?

**KQ 2:** What is the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI?

**a.** Do effectiveness and comparative effectiveness vary by rehabilitation timing, setting, intensity, duration, or composition?

**b.** Do effectiveness and comparative effectiveness vary by injury characteristics?

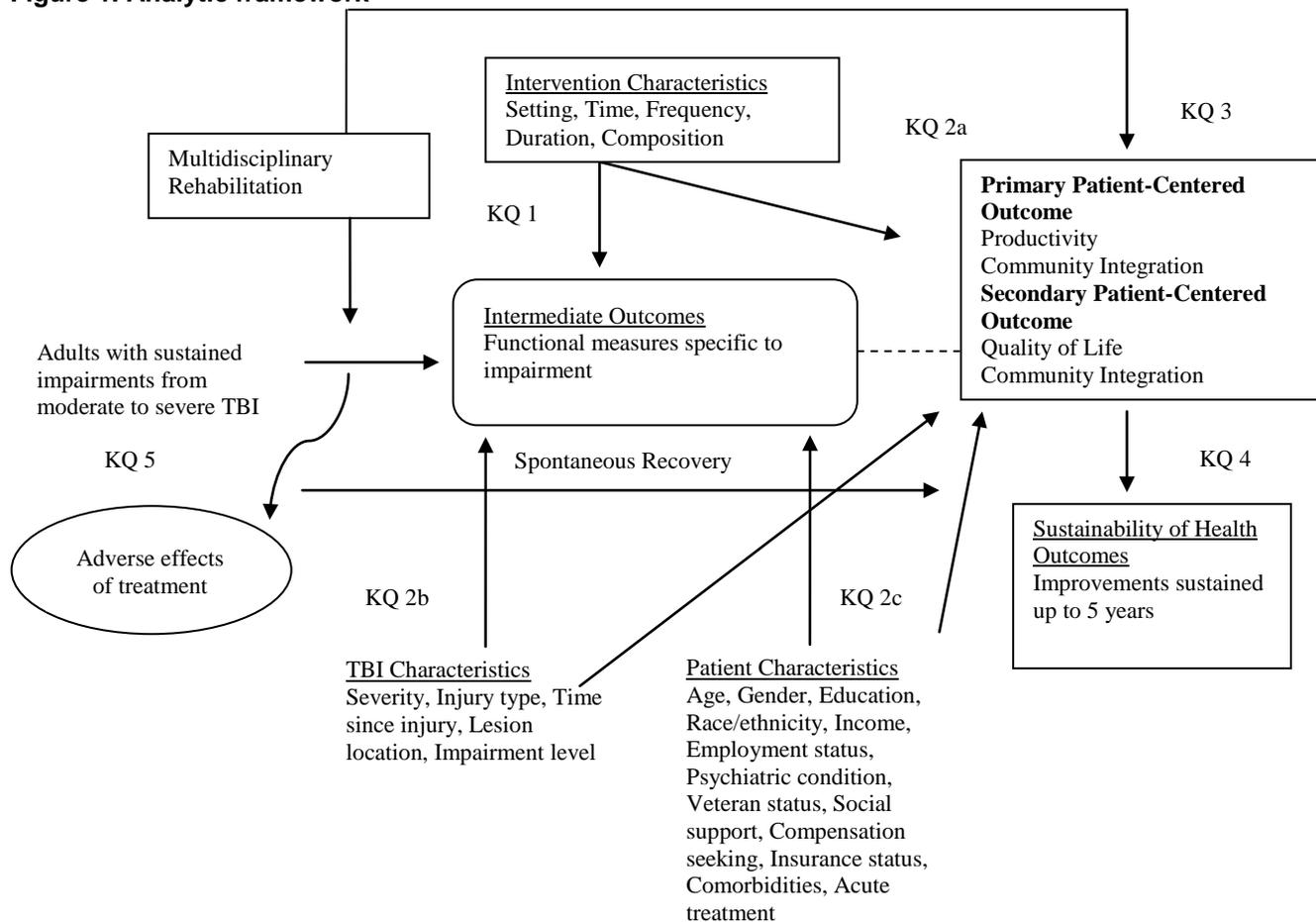
**c.** Do effectiveness and comparative effectiveness vary by patient characteristics, preinjury or postinjury?

**KQ 3:** What evidence exists to establish a minimum clinically important difference in community reintegration as measured by the Mayo-Portland Adaptability Inventory-4 for postacute rehabilitation for TBI in adults?

**KQ 4:** Are improvements in outcomes achieved via multidisciplinary postacute rehabilitation for TBI sustained over time?

**KQ 5:** What adverse effects are associated with multidisciplinary postacute rehabilitation for TBI?

**Figure 1. Analytic framework**



KQ = Key Question; TBI = traumatic brain injury

## Comparative Effectiveness Review Findings

The literature search conducted for the CER covered material indexed through January 2012. Our intent was to identify and synthesize data from relevant comparative effectiveness research on multidisciplinary rehabilitation programs to inform treatment decisions. The primary outcome of interest was participation in community life as indicated by productivity or select measures of community integration.

For KQ 1, we found that multidisciplinary postacute rehabilitation programs for impairments from moderate to severe TBI varied widely in terms of populations targeted, setting, program intensity and duration, and timing of intervention. Clear categorization of all studied interventions was not possible. However, the most frequently studied programs are those based upon the comprehensive holistic day treatment model of care. These programs maintained a similar approach and mode of delivery. Individuals were enrolled in and progressed through structured intensive day-treatment programs in small groups of individuals that received several hours of treatments per day, several days per week. Treatment was delivered largely through group sessions, while maintaining an emphasis on addressing individual needs. Emphases included self-awareness of impairments and compensatory approaches to retraining, with vocational rehabilitation another key element.

From the evidence synthesized for KQ 2, we were unable to draw broad conclusions about effectiveness or comparative effectiveness of multidisciplinary rehabilitation programs. We found that a Comparative Effectiveness Review on such complex interventions led to conclusions about the very specific populations and interventions studied:

- We found insufficient evidence assessing effectiveness for productivity or community integration.
- We found low-strength evidence that gainful employment or return to military fitness did not differ significantly at 1 year posttreatment between an 6-week inpatient hospital treatment and a 8-week limited home-based treatment. Participants were active duty military patients with closed head injuries and with relatively mild impairment levels who were treated within 3 months of injury.
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effectiveness, and identified few well-designed studies to address comparative effectiveness. Applicability of those studies also appears problematic. However, our CER findings should not be misunderstood to be evidence of ineffectiveness, but should instead provide justification for additional research in order to further establish understanding of these complex interventions.

To guide the development of additional comparative effectiveness research on this topic, this FRN project aims to identify specific evidence gaps and prioritize FRNs with research design considerations likely to advance the field.

## Evidence Gaps and Research Question Development

As with much of the research on functional therapies, many studies of multidisciplinary rehabilitation for adults with moderate to severe TBI exhibited problems with design and conduct. Our original report included general recommendations to fill evidence gaps on this topic. To elaborate on these recommendations, we translated specific evidence gaps into research questions. Research questions are presented in two categories: methodological research questions that need to be addressed to enhance the usefulness of current topical research, and topical research questions not adequately addressed within the current literature:

### Methodological Research Questions

1. What taxonomies of moderate to severe TBI impairments should be used in research to encourage consistency and comparability across studies?
2. How should the severity of specific impairments be assessed and reported in effectiveness research to encourage consistency and comparability across studies?
3. How should the severity of overall impairments be assessed and reported in effectiveness research to encourage consistency and comparability across studies?
4. What framework describing postacute rehabilitation for moderate to severe TBI should be used in research to encourage consistency and comparability across studies?
5. What taxonomy for postacute rehabilitation for moderate to severe TBI should be used in research to encourage consistency and comparability across studies?
6. How should interventions be defined to encourage consistency and comparability across studies and support replicability?
  - a. Comprehensive programs
  - b. Individual components of comprehensive programs
7. What are the valid and reliable instruments used to measure *patient-centered outcomes*?
  - a. What is the MCID for each of these valid and reliable instruments?
  - b. What cut points should be used to describe clinically meaningful categories in the scale scores created by these instruments?
  - c. What are the advantages and disadvantages to using MCIDs in research on this topic?
8. What are the valid and reliable instruments used to measure *intermediate outcomes* when evaluating the effectiveness and comparative effectiveness of individual components of comprehensive programs or single-impairment therapies?
9. Which intermediate outcomes meet criteria for *surrogate patient-centered outcomes*?

10. What confounding variables (e.g., family support, patient engagement, concomitant therapies, comorbidities), and effect modifiers (e.g., education level, preinjury employment status, age group) should be addressed and reported in effectiveness research?
11. What specific data should be reported in effectiveness studies?

## **Topical Research Questions**

1. What is the effectiveness of postacute rehabilitation for moderate to severe TBI?
2. What is comparative effectiveness of postacute rehabilitation for moderate to severe TBI?
3. What is the marginal benefit from specific components of comprehensive programs (e.g., case management) delivered in the appropriate stage of recovery?
4. Do sustained changes in patient-centered outcomes differ by the duration, intensity, and frequency of examined interventions?
5. Which patient characteristics are associated with patient-centered outcomes (comorbidities age, functional status, time since injury, impairment type, concomitant treatments, etc.)?
6. How do patient-centered outcomes differ depending on the setting in which rehabilitation is provided?

## Methods

We used a deliberative process to identify and prioritize research questions relevant to the evidence gaps identified in the recently completed draft CER “Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults.”<sup>1</sup> Figure 2 illustrates the eight steps used to accomplish the objectives of this project.

### Engagement of Stakeholders

We recruited a diverse stakeholder panel whose members represented various perspectives relevant to the topic. We followed Agency for Healthcare Research and Quality (AHRQ) guidance on stakeholder engagement for recruitment and communication.<sup>2</sup> We sought to recruit stakeholders who were actively interested in multidisciplinary rehabilitation programs for TBI impairments and who wished to help shape future research priorities. We identified potential stakeholders via several means. We sought recommendations from the CER project team, including select Key Informants, Technical Expert Panel members, and peer and public reviewers. We also identified stakeholders who were serving on panels from related AHRQ FRN projects or who were listed in the Effective Health Care Contacts Database.<sup>3</sup>

Research representatives were national experts who were familiar with: (1) evidence-based medicine; (2) the obstacles often associated with conducting well-designed research on this complex condition; and (3) interventions from the fields of physical medicine and rehabilitation, neuropsychology, and speech-language pathology.

We invited participation from representatives from organizations supporting or conducting relevant research including United States Department of Veterans Affairs, United States Department of Defense, National Institute on Disability and Rehabilitation Research, National Institute of Neurological Disorders and Stroke, the American Academy of Physical Medicine and Rehabilitation, and the American Congress of Rehabilitation Medicine. We also invited policy and payer representation from the Centers for Medicare and Medicaid Services. Many stakeholders were also involved in the CER process as Key Informants, Technical Expert Panel members, or peer reviewers. This made engaging them as stakeholders challenging, because the timing of the FRN project overlapped with finalization of the CER.

### Handling Conflicts of Interest

We collected disclosures of conflicts of interests from all stakeholders. Disclosed interests did not bar any stakeholders from participation, but allowed the Evidence-based Practice Center (EPC) to evaluate contributions based upon possible conflicts. Stakeholders used a Web-based survey to rank research questions during the prioritization exercise, thus researchers and funders were blind to the others’ stated opinions.

### Refinement of Research Questions

We provided stakeholder panel members with a preliminary set of research questions prior to conference calls. During conference calls, we sought stakeholder input to further refine the research questions (i.e., organization and wording of the questions, identification of additional research questions, and elimination of research questions with limited clinical value). To facilitate this input, we provided stakeholders in advance with background material including the draft CER executive summary. We conducted three conference calls with available stakeholders during May 2012. A total of 10 stakeholders participated in the calls. All participants provided

input on the calls. We revised the preliminary questions based on these discussions, and we invited stakeholders to edit or comment on the revised set of questions.

We also revised the preliminary questions in light of recent and ongoing work. For instance, the National Institute of Neurological Disorders and Stroke Common Data Elements project for TBI<sup>4</sup> has addressed several of the limitations we found in the current literature concerning poor reporting of patient and injury characteristics, as well as inconsistent use of valid and reliable outcomes measures. We therefore excluded those questions from the ranking process. The revised set of research questions for prioritization appears in Appendix A.

## Prioritization

We asked stakeholders to prioritize these research questions according to specified criteria based on the potential impact of future research on that question. These criteria have been operationalized into seven components specific to EPC FRN projects. These components, called “Potential Value Criteria,” are as follows<sup>5</sup>:

- Potential for significant health impact on the current and future health status of people with respect to burden of the disease and health outcomes: mortality, morbidity, and quality of life.
- Potential to reduce important inappropriate (or unexplained) variation in clinical practices known to relate to quality of care. Potential to resolve controversy or dilemmas in what constitutes appropriate health care. Potential to improve decisionmaking for patient or provider, by decreasing uncertainty.
- Potential for significant (nontrivial) economic impact related to the costs of health service: to reduce unnecessary or excessive costs; to reduce high costs due to high volume use; to reduce high costs due to high unit cost or aggregate cost. Costs may impact consumers, patients, health care systems, or payers.
- Potential risk from inaction: Unintended harms from lack of prioritization of proposed research; opportunity cost of inaction.
- Addresses inequities, vulnerable, diverse populations (including issues for patient subgroups); potential to reduce health inequities.
- Potential to allow assessment of ethical, legal, social issues pertaining to the condition.
- Potential for new knowledge (Research would not be redundant; Question not sufficiently researched, including completed and in-process research; Utility of available evidence limited by changes in practice, e.g., disease detection or evolution in technology).

We developed a Web-based survey using SurveyMonkey to collect stakeholder prioritization of the research gap questions.<sup>6</sup> All 10 stakeholders who completed disclosure statements (no more than 9 were non-Federal employees) were invited to rank research questions identified via the stakeholder conference calls. These stakeholders numerically ranked their top three of seven methodological research questions, and their top three of six topical research questions.

Stakeholder rankings were weighted according to their assigned numerical ranking. If a stakeholder assigned a question the number one priority, that question received three points; number two ranking received two points; number three ranking received one point. Three of the five respondents misunderstood the instructions and gave identical rankings to several questions. We evaluated the order of these rankings to determine the intended highest priority questions and averaged the weighted points (e.g., if a respondent gave three questions a number one priority, we gave each of those questions two points; questions ranked as second and third priorities would get no points). We identified natural breakpoints in the weighted rankings that separated

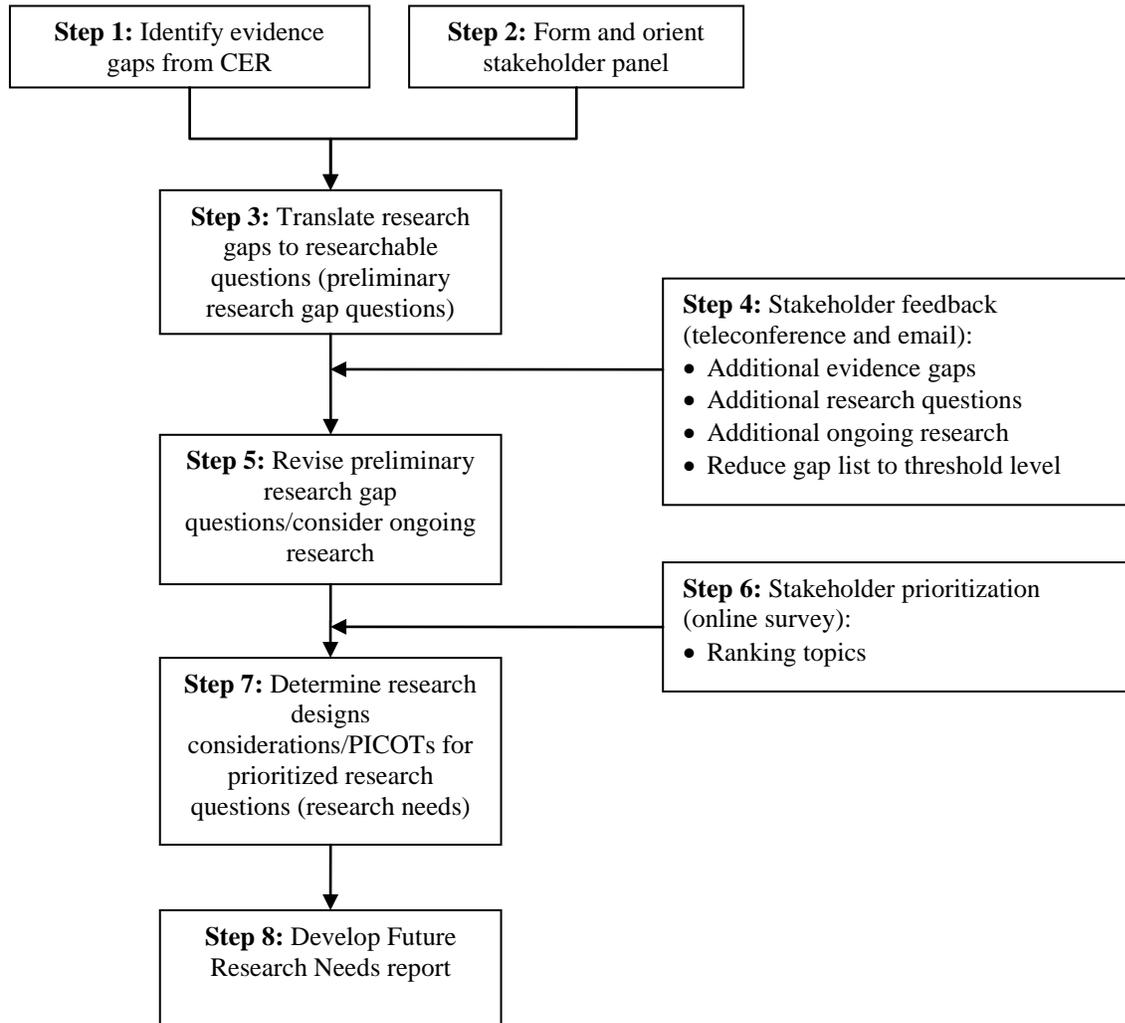
high-, moderate-, and low-priority research questions. Highly prioritized research questions were considered research needs.

We then evaluated the feasibility criteria for research needs. We framed feasibility in terms of anticipated research designs. For example, factors that affect the feasibility of conducting randomized controlled trials include the sample size needed for the outcome, the size of the available pool of potential subjects, followup duration, willingness to randomize, and applicability issues. In contrast to randomization and applicability, observational studies face feasibility issues related to measuring potential confounding or effect modifying variables.

## **Research Design Considerations**

We generated research design considerations for identified research needs. For methodological research needs, we provided context and described resources and research design considerations potentially useful to researchers, facilitators, and funders of this type of research. For topical research needs, we highlighted the relevant element(s) of the PICOTS (population, intervention, comparison, outcome, timing, and setting), provided context, described related ongoing research, and discussed potential research designs. Because more than one research design can be applied to an individual research need, we discussed the advantages and disadvantages of different options. These discussions were guided by a recent AHRQ report describing a framework to use in considering study designs for future research.<sup>7</sup> We did not consult with stakeholders for input on research design considerations.

**Figure 2. Project flow**



CER = Comparative Effectiveness Review; FRN = Future Research Needs; PICOTS = population, intervention, comparison, outcome, timing, and setting

# Results

## Research Needs

### Prioritization Results

Stakeholders separately ranked methodological and topical research questions. Of the 10 stakeholders invited to participate in the ranking process, 5 ranked methodological research questions and 4 ranked topical research questions. We analyzed weighted stakeholder rankings for each research question to identify natural breakpoints (Table 1). High-priority research questions were deemed research needs.

### Ongoing Studies

We conducted a search for ongoing studies in ClinicalTrials.gov (search strategy appears in Appendix B). Our search identified 289 studies. Thirteen of these studies (Appendix C) were not yet published and relevant to the scope of our CER. These studies will provide valuable information, but we did not believe any ongoing study would sufficiently address identified future research questions.

**Table 1. Stakeholder prioritization of research gap questions**

| Question Ranking*   | Total (Points) | PICOTS Element |
|---|----------------|----------------|
| <b><i>Methodological Topics Needing Consensus (n=5)</i></b>   |                |                |
| <b>Tier 1: High Priority</b>  |                |                |
| Which <u>patient characteristics</u> confound/modify effectiveness of rehabilitation programs?  | 8              | P              |
| What outcomes of multidisciplinary rehabilitation are most important to: <ul style="list-style-type: none"> <li>• Patients</li> <li>• Families</li> <li>• Payers</li> </ul>   | 7              | O              |
| <b>Tier 2: Moderate Priority</b>  |                |                |
| How should patient readiness for multidisciplinary rehabilitation programs be measured?   | 5.8            | P, I           |
| Which injury characteristics confound/modify effectiveness of rehabilitation programs?  | 4.8            | P              |
| What typology should be used to classify multidisciplinary rehabilitation programs?   | 3              | I              |
| <b>Tier 2: Low Priority</b>   |                |                |
| Which intermediate outcomes adequately predict patient-centered outcomes (surrogate outcomes)?  | 1              | O              |
| What are the MCIDs for outcomes instruments? <ol style="list-style-type: none"> <li>a. What are the advantages and disadvantages to using MCIDs in research on this topic?</li> </ol> Should they be used to measure program effectiveness? | 0.3            | O              |

**Table 1. Stakeholder prioritization of research gap questions (continued)**

| Question Ranking*   | Total (Points) | PICOTS Element |
|---|----------------|----------------|
| <i>Topical Questions Needing Trials (n=4)</i>   |                |                |
| <b>Tier 1: High Priority</b>  |                |                |
| <b>Timing:</b> At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?   | 7.5            | T              |
| Which multidisciplinary rehabilitation programs are “promising practices?”<br>a. What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?<br>b. What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?<br>c. Which patients (subgroups) appear to benefit most by various multidisciplinary rehabilitation programs?<br>d. What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs? | 5.5            | I              |
| <b>Sustainability and Followup:</b> Are benefits received from multidisciplinary rehabilitation programs sustained over the long-term?<br>• What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods post rehabilitation?  | 5              | O, T           |
| <b>Tier 2: Moderate Priority</b>  |                |                |
| <b>Intervention Characteristics:</b> Which intervention characteristics predict response in various forms of multidisciplinary rehabilitation programs?   | 3.3            | I              |
| <b>Multidisciplinary rehabilitation program versus accessible rehabilitation:</b> What is the comparative effectiveness of various types of multidisciplinary rehabilitation programs vs. rehabilitation typically covered by third party payers?   | 2.3            |                |
| <b>Tier 3: Low Priority</b>   |                |                |
| <b>Subgroups:</b> Does the efficacy of specific multidisciplinary rehabilitation programs vary across patient subgroups?  | 0.3            | P              |

MCIDS = minimum clinically important differences; PICOTS = population, intervention, comparison, outcome, timing, and setting

\*Rankings were weighted to create a total point score by assigning questions ranked #1 by stakeholders with 3 points, questions ranked #2 with 2 points, questions ranked #3 by stakeholders with 1 point. A forced ranking was used with responses that recording duplicate ratings.

## Methodological Research Needs

A natural breakpoint in weighted rankings revealed two methodological research needs. Addressing methodological research needs will enhance the utility and translation of current and future research on multidisciplinary rehabilitation programs for sustained impairments from moderate to severe TBI in adults:

- What outcomes of multidisciplinary rehabilitation are most important to:
  - Patients
  - Families
  - Payers
- Which patient characteristics confound/modify effectiveness of rehabilitation programs?

Methodological research needs pertain to identifying outcomes that are important to patients, families, and payers, and to identifying patient characteristics that influence response to rehabilitation.

## Considerations for Potential Research Designs

There are several ways that these methodological research needs could be addressed. Systematic reviews, epidemiological studies, and/or qualitative research would all assist in improving the understanding with regard to valued outcomes and factors than confound or

modify the effect of TBI rehabilitation. One way to identify specific outcomes valued by patients may be to review the literature or secondary databases about TBI rehabilitation programs that use shared decisionmaking or goal setting among patients, families, and providers. Qualitative research would also be useful. Focus groups, for example, with representatives of patients, families, and payers – in separate focus groups- would help to identify these outcomes. Several patient and family focus groups would be necessary due to the wide range of impairment types and levels resulting from moderate to severe TBI. Preferred outcomes are likely associated with patient impairment types and levels at rehabilitation initiation.

Patient characteristics associated with the effectiveness of rehabilitation programs could be identified through similar methods. This process would benefit first from a systematic literature review. Several studies that examine patient characteristics and their influence on outcomes are available. A systematic review is not likely to provide the complete picture of confounding and effect modifying factors. Analysis of secondary databases and post hoc analysis of effectiveness studies establishing potential relationships between patient characteristics and patient outcomes should be included in such a systematic review. By definition, multidisciplinary rehabilitation programs involve several provider types; therefore, a multidisciplinary approach to consensus development is essential. Participants should include clinical experts and researchers with expertise in clinical outcomes, epidemiology, biostatistics, and health services research.

## **Topical Research Needs**

A natural breakpoint in the weighted rankings revealed three prominent topical research needs. These primarily addressed the PICOTS elements of interventions, outcomes, and timing; Addressing these issues will enhance understanding of efficacy and comparative effectiveness, which was limited in the draft CER.

### **First Topical Research Need**

Research Question: Which multidisciplinary rehabilitation programs are “promising practices?”

- a. What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?
- b. What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?
- c. Which patients (subgroups) appear to benefit most by various multidisciplinary rehabilitation programs?
- d. What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?

The draft CER and peer review of that draft emphasized the limited value of rigorous Comparative Effectiveness Reviews on this topic given the complexity of rehabilitation programs for TBI impairments and the current status of this literature.

### **Research Design Considerations**

The draft CER and peer review of that draft emphasized the limited value of rigorous Comparative Effectiveness Reviews on this topic given the complexity of rehabilitation programs for TBI impairments and the current status of this literature. As topics for Comparative Effectiveness Reviews have expanded beyond pharmaceutical interventions, alternative approaches have been proposed to synthesize research on complex interventions (characterized

as programs in which effects are dependent on context and implementation). “Realist reviews” may be an option better suited to such topics.<sup>8</sup> These reviews are rigorous systematic reviews, but focus more on explaining how, when, and why certain interventions may work or not work. This approach to a systematic review provides improved understanding of interventions and their populations and therefore may be a good fit for complex interventions such as rehabilitation.

Realist reviews seek to provide an explanatory analysis discerning what works for whom and under what circumstances. This information can help strengthen understanding of programs and inform efficient and effective implementation.<sup>8</sup> Although realist reviews cannot achieve the goal of Comparative Effectiveness Reviews, which is, ideally, to identify what works and what does not, they can generate information that spurs hypotheses from which to design comparative effectiveness studies. A realist review could be useful in identifying promising practices. Research design considerations for a review of this type are described in Table 2.

**Table 2. First topical research need research design considerations**

| <b>Research Question: Which multidisciplinary rehabilitation programs are “promising practices?”</b>  |  |
|---|--|
| <b>a. What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?</b><br><b>b. What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?</b><br><b>c. Which patients (subgroups) appear to benefit most by various multidisciplinary rehabilitation programs?</b><br><b>d. What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?</b> |  |
| <b>Considerations</b>   | <b>Realist Review</b>  |
| Design Description  | Systematic review of the literature that seeks to provide an explanatory analysis discerning what works for whom and under what circumstances.   |
| Population  | Studies evaluating rehabilitation effectiveness.   |
| Intervention  | Multidisciplinary rehabilitation program.  |
| Comparator  | Any control (may include uncontrolled studies).  |
| Outcomes  | Any outcomes measured in original studies.   |
| Advantages for Producing a Valid Result   | Results will be descriptive and explanatory and will not lead to definitive conclusions about efficacy or comparative effectiveness, but provide a more in-depth understanding of how, when, and why certain rehabilitation programs work and in which patients. |
| Resource use, size, and duration  | Minimal, study can be conducted by secondary data analysis. Resource use includes investigator time and related resources. Investigator time will be significant.  |
| Ethical, legal, and social issues   | No ethical, legal, or social issues.   |
| Availability of data/ability to recruit   | Good, several studies are available. However, data will be limited to what is reported in original studies.  |

## **Second Topical Research Need**

Research Question: At what stage of recovery do multidisciplinary rehabilitation programs offer patients the best chance of improvement?

Understanding the ideal timing to enroll those with impairments from moderate to severe TBI into rehabilitation programs is our second topical research need. This question was addressed by the CER KQs. However, data was too limited assess the influence of rehabilitation program timing. The CER did demonstrate the wide range of multidisciplinary rehabilitation programs studied. Some are aimed at those with recent injuries, others to those that have achieved medical stability, and others to those with chronic impairments. These programs likely vary widely with regard to content and approach; however, a better understanding about the timing of specific types of rehabilitation programs could provide important information for clinical decision making. This is especially critical in an environment of limited resources, because payers want to support rehabilitation when it can be most beneficial.

## Research Design Considerations

This question was explored in the CER. Unfortunately, evidence was insufficient to draw conclusions. To more definitively determine if earlier initiation of multidisciplinary rehabilitation programs improve patient outcomes, controlled studies should test the effect of rehabilitation timing (in terms of functional status and/or time-since-injury) on outcomes. A few approaches could be utilized including randomized controlled trials, nonrandomized trials, and prospective cohort studies. Table 3 compares the research design considerations of these three approaches.

**Table 3. Second topical research need research design considerations**

| <b>Research Question: At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?</b> |   |   |  |
|--|---|---|--|
| <b>Considerations</b>  | <b>RCT</b>  | <b>Nonrandomized Controlled Trial</b>   | <b>Prospective Cohort</b>  |
| Design Description   | Individual patients randomly assigned to rehabilitation programs initiated at various stages.   | Individual rehabilitation centers assigned to multidisciplinary rehabilitation programs initiated at various stages.  | Individuals allowed to select timing of initiating multidisciplinary rehabilitation program.   |
| Population   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.  |
| Intervention   | Multidisciplinary rehabilitation program begun earlier or later in recovery.  | Multidisciplinary rehabilitation program begun earlier or later in recovery.  | Multidisciplinary rehabilitation program begun earlier or later in recovery.   |
| Comparator   | Rehabilitation program initiated once patient medically stable.   | Rehabilitation program initiated once patient medically stable.   | Rehabilitation program initiated once patient medically stable.  |
| Outcomes   | Participation; quality of life  | Participation; quality of life  | Participation; quality of life   |
| Timing   | Followup should extend through at least one-year after initiation of rehabilitation program.  | Followup should extend through at least one-year after initiation of rehabilitation program.  | Followup should extend through at least one-year after initiation of rehabilitation program.   |
| Setting  | Rehabilitation center   | Rehabilitation center   | Rehabilitation center  |
| Advantages for Producing a Valid Result  | This design, if feasible, is likely to produce the most valid results by minimizing bias from observed and unobserved variables. However, generalizability is likely to be low. | This design is more feasible than a RCT, but validity will be hampered. It will be difficult to determine if differences are due to timing or to rehabilitation center. | This design is most feasible; however risk of confounding will be high. Investigators should be careful to collect data necessary to statistically adjust for known confounders and effect modifiers. Unknown confounders also likely to be an issue. Generalizability should be high. |

**Table 3. Second topical research need research design considerations (continued)**

| <b>Research Question: At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?</b> |   |  |   |
|--|---|--|---|
| <b>Considerations</b>  | <b>RCT</b>  | <b>Nonrandomized Controlled Trial</b>  | <b>Prospective Cohort</b>   |
| Resource use, size and duration  | Likely necessary to recruit large samples and follow for significant length of time to insure adequate power; Intervention is also resource intensive involving multidisciplinary rehabilitation teams. | Similar to RCT   | Sample size will need to be larger than experimental designs given heterogeneity of population and number of confounding/effect modifying variables. Investigators should perform power calculations. |
| Ethical, legal, and social issues  | Ethical challenges exist. Cognitive and behavioral impairment are a common TBI impairment. Additionally, earlier rehabilitation may be seen as superior.  | If standard timing of rehabilitation differs across rehabilitation centers, recruitment should not be difficult. | No major ethical or legal challenges.   |
| Availability of data/ability to recruit  | Poor. Intervention requires significant time commitment; patients may be unwilling to be randomized to later rehabilitation program.  | Better than RCT, however same challenges remain.   | No major challenges to recruitment.   |

RCT = randomized controlled trial; TBI = traumatic brain injury

### **Third Topical Research Need**

Research Question: Are benefits received from multidisciplinary rehabilitation programs sustained over the long term?

- a. What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods postrehabilitation?

The last identified research need also relates to timing. Our stakeholders were very concerned about improving evidence assessing whether and how TBI patients can maintain the gains made in rehabilitation. The CER addressed this question and found some evidence that rehabilitation gains were sustained in the few studies that included longer term followup. However, the strength of this evidence was low, timeframes rarely went beyond 1-year and study results may have limited applicability. Stakeholders suggested that followup care is beneficial to maintaining rehabilitation gains, but little is known about how and why these benefits are conferred. None of the rehabilitation programs we examined for the CER had formal followup rehabilitation components. Additional research to examine the benefits of followup rehabilitation sessions would inform decisionmaking.

### **Research Design Considerations**

Table 4 compares the research design considerations of these three approaches. Research design considerations are similar to those addressing the previous research need about rehabilitation timing.

**Table 4. Third topical research need research design considerations**

| <b>Research Question: Sustainability &amp; Followup: Are benefits received from multidisciplinary rehabilitation programs sustained over the long-term?</b>        |   |   |   |
|--|---|---|---|
| <b>a. What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods post rehabilitation?</b> |   |   |   |
| <b>Considerations</b>  | <b>RCT</b>  | <b>Nonrandomized Controlled Trial</b>   | <b>Prospective Cohort</b>   |
| Design Description   | Individual patients randomly assigned to rehabilitation programs with varying levels of followup.   | Individual rehabilitation centers assigned to multidisciplinary rehabilitation programs with varying levels of followup.  | Individuals select level of followup included with multidisciplinary rehabilitation program.  |
| Population   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.   | Patients with sustained impairments from moderate to severe TBI; limited to closed head injuries.   |
| Intervention   | Multidisciplinary rehabilitation program with varying levels of followup.   | Multidisciplinary rehabilitation program with varying levels of followup.   | Multidisciplinary rehabilitation program with varying levels of followup.   |
| Comparator   | Multidisciplinary rehabilitation program with no followup.  | Multidisciplinary rehabilitation program with no followup.  | Multidisciplinary rehabilitation program with no followup.  |
| Outcomes   | Participation; quality of life  | Participation; quality of life  | Participation; quality of life  |
| Timing   | Followup should extend 2-5 years to fifteen years after program initiation.   | Followup should extend 2-5 years to fifteen years after program initiation.   | Followup should extend 2-5 years to fifteen years after program initiation.   |
| Setting  | Rehabilitation center   | Rehabilitation center   | Rehabilitation center   |
| Advantages for Producing a Valid Result  | This design, if feasible, is likely to produce the most valid results. However, generalizability is likely to be low.   | This design is more feasible than a RCT, but validity will be hampered. It will be difficult to determine if differences are due to degree of followup or to rehabilitation center. | This design is most feasible; however risk of confounding will be high. Investigators should be careful to collect data necessary to statistically adjust for known confounders and effect modifiers. Unknown confounders are also likely to be an issue. |
| Resource use, size and duration  | Likely necessary to recruit large samples and follow for significant length of time; Power calculations should be performed. Loss to followup likely to be significant. Intervention itself and monitoring fidelity to protocol are resource intensive. | Similar challenges to RCT.  | Sample size will need to be larger than randomized designs given heterogeneity of population and number of confounding/effect modifying variables. Power calculations should be performed. Loss to followup likely to be significant.                     |

**Table 4. Third topical research need research design considerations (continued)**

| <b>Research Question: Sustainability &amp; Followup: Are benefits received from multidisciplinary rehabilitation programs sustained over the long-term?</b>        |   |   |  |
|--|---|---|--|
| <b>a. What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods post rehabilitation?</b> |   |   |  |
| <b>Considerations</b>  | <b>RCT</b>  | <b>Nonrandomized Controlled Trial</b>                                   | <b>Prospective Cohort</b>  |
| Ethical, legal, and social issues  | Ethical challenges exist. Cognitive and behavioral impairment are a common impairment resulting from TBI. Additionally, followup rehabilitation sessions may be seen as superior. | Fewer challenges in recruiting rehabilitation centers than individuals. | No major ethical or legal challenges.  |
| Availability of data/ability to recruit  | Poor. Intervention requires significant time commitment; patients may be unwilling to be randomized to no followup rehabilitation program.  | Better than RCT, however same challenges remain.                        | Fewer challenges to recruitment. Patients may be unwilling to commit to no followup rehabilitation programs. |

RCT = randomized controlled trial; TBI = traumatic brain injury

## Discussion

This FRN project refined and prioritized research needs relevant to the KQs addressed in the draft CER, “Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults.”<sup>1</sup> We conducted a deliberative process to refine and expand research gaps identified in the CER through conversations with stakeholders who represented various perspectives and expertise on the topic. This process identified seven methodological and six topical research questions thought to address identified evidence gaps. We then asked stakeholders to rank research questions according to their potential impact. The highly ranked questions were deemed research needs. Stakeholders prioritized two methodological and three topical research needs.

Addressing methodological research needs will enhance the utility and comparability of future studies of multidisciplinary rehabilitation for moderate to severe TBI. These needs involve identifying patient centered outcomes and patient characteristics associated with response to rehabilitation.

Identified research needs demonstrate the importance of an enhanced understanding of (1) how and why multidisciplinary rehabilitation programs benefit specific types of patients and (2) the timing of rehabilitation that may be most beneficial. Future studies of multidisciplinary rehabilitation programs should be designed to pay close attention to reducing bias as much as possible for the selected research design. Studies should be adequately powered to test hypothesized relationships, including among subgroups.

While a strength of this project is the intended variety of perspectives brought by broad stakeholder participation, we were not able to collect a representative perspective from a larger sample of stakeholders and had a low response rate to our stakeholder invitations and ranking process. This is a major limitation. The stakeholders participating in this project represented various perspectives on multidisciplinary rehabilitation programs for TBI. However, the prioritized research needs reflect the opinions of these stakeholders and may not be applicable to the broader population of stakeholders on this topic.

Our stakeholder panel was also limited in size by standards and guidelines for statistical surveys administered by the Office of Management and Budget. These guidelines require compliance with the Paperwork Reduction Act and Information Collections Policy (44 USC 3501-3520).<sup>9</sup> The Act was designed to (1) minimize the paperwork burden on the public; (2) assure that high quality data are obtained, and (3) minimize costs. The Act requires special approval for projects that wish to include more than nine non-government participants; however, the approval process exceeded the length of time available to complete this FRN project.

Finally, this CER and related FRN project overlapped with several other projects that tapped the same group of stakeholders. This could explain the limited availability and interest in participation. Stakeholder discussions emphasized the need for federal agencies to work together to understand ongoing activities within each agency to avoid duplication of effort.

Future studies of multidisciplinary rehabilitation programs should seek to reduce bias as much as possible for the particular research design used. Literature examined for the draft CER rarely provided adequate and consistent measurement and reporting of variables thought to confound or modify the effect of multidisciplinary rehabilitation programs, but because the ongoing Common Data Element efforts appear to sufficiently address this concern, we did not include this methodological research question in our list prioritized by stakeholders. One study currently underway (NCT01565551) is testing the use of Common Data Element recommendations. Investigators interested in this topic should follow these ongoing efforts.

Further, studies should be adequately powered to test hypothesized relationships. Power calculations that take into consideration any subgroup analysis that may be performed are especially encouraged.

Additionally, the quality of comparative effectiveness research on multidisciplinary rehabilitation for impairments from moderate to severe TBI could be greatly improved through more precise intervention definitions and the construction of a topology of the various approaches to multidisciplinary rehabilitation programs. Guidance is available to researchers regarding how to better describe interventions in order to enhance the quality of comparative effectiveness studies and permit replicability.<sup>10</sup> Interventions that are founded on theory, manualized, and utilize fidelity checks to ensure proper implementation are most likely to result in studies with valid results. Reporting guidance in published comparativeness studies with particular attention to intervention definition is also available. The Consolidated Standards of Reporting Trials (CONSORT) statement for nonpharmacologic interventions could guide the data collected and reported in effectiveness research.<sup>11</sup> The CONSORT statement specifically describes elements of interventions that should be included. The Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) statement, designed for public health interventions, also provides a good explanation of the types of information about interventions that should be captured and reported.<sup>12</sup>

Lastly, one stakeholder's comment provided in the ranking survey illustrates the context of current state of research on this topic. This stakeholder felt that ranking the topical research questions was not possible, commenting:

“I have trouble getting invested in any of these questions in the current real world in which we live. Based on this review, we have very tenuous evidence of the effectiveness of such programs in the first place, and no typology of the programs being evaluated to even know whether they exist in categories or each is idiosyncratically developed to meet the needs of the specific patients and payers who happen to be present locally. The above are all much more nuanced questions that I don't believe can be answered in the foreseeable future. The evidence to answer them does not exist and it will require a major investment in primary treatment research to generate enough evidence to conduct productive meta-analyses or CER reviews. I think there is limited value to listing the research questions that in theory need to be answered when they are so far removed from the research currently being supported.”

This comment mirrors another stakeholder discussion suggesting that preliminary research questions focused on the effectiveness of rehabilitation programs were beyond the current science on the topic. This stakeholder felt that a better understanding of individual interventions is first required before considering programs as a whole. In any case, an improved understanding of multidisciplinary programs and the specific components of these programs appears imperative to advance this field. While current efforts are underway to enhance this understanding, TBI rehabilitation would benefit from a coordinated research agenda and funding to support additional efforts to enhance our understanding of multidisciplinary rehabilitation programs.

## Conclusions

This FRN project identified several research needs thought relevant by a select group of stakeholders to move the field forward. The first research need was not directly addressed in our CER and therefore may need a systematic review to determine more specifically what these research gaps are:

- What outcomes of multidisciplinary rehabilitation are most important to:
  - Patients
  - Families
  - Payers

Remaining research needs were questions that would have been covered in the original CER, but evidence was insufficient and/or conclusions had limited applicability:

- Which patient characteristics confound/modify effectiveness of rehabilitation programs?
- Which multidisciplinary rehabilitation programs are “**promising practices?**”
  - What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?
  - What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?
  - Which patients (**subgroups**) appear to benefit most by various multidisciplinary rehabilitation programs?
  - What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?
- **Timing:** At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?
- **Sustainability and followup:** Are benefits received from multidisciplinary rehabilitation programs sustained over the long term?
  - What level and type of followup care allows for maintenance of or prevents deterioration of rehabilitation gains at given time periods postrehabilitation?

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## Abbreviations

|        |  |
|--------|--|
| AHRQ   | Agency for Healthcare Research and Quality                         |
| CER    | Comparative Effectiveness Review                                   |
| EPC    | Evidence-based Practice Center                                     |
| FRN    | Future Research Needs  |
| KQ     | Key Question   |
| MCID   | Minimum clinically important difference                            |
| PICOTS | Population, intervention, comparison, outcome, timing, and setting |
| RCT    | Randomized controlled trial  |
| TBI    | Traumatic brain injury   |

# Appendix A. Research Questions for Prioritization

## Methodological Research Questions

1. How should patient readiness for multidisciplinary rehabilitation programs be measured?
2. What outcomes of multidisciplinary rehabilitation are most important to:
  - Patients
  - Families
  - Payers
3. MCIDs
  - What are the minimum clinically important differences (MCIDs) for outcomes instruments?
  - What are the advantages and disadvantages to using MCIDs in research on this topic?
  - Should they be used to measure program effectiveness?
4. Which *intermediate outcomes* adequately predict *patient-centered outcomes* (surrogate outcomes)?
5. Which injury characteristics confound/modify effectiveness of rehabilitation programs?
6. Which patient characteristics confound/modify effectiveness of rehabilitation programs?
7. What typology should be used to classify multidisciplinary rehabilitation programs?

## Topical Research Questions

1. Which multidisciplinary rehabilitation programs are “**promising practices?**”
  - a. What benefits are experienced by patients participating in various multidisciplinary rehabilitation programs?
  - b. What outcomes appear to be most improved by various multidisciplinary rehabilitation programs?
  - c. Which patients (**subgroups**) appear to benefit most by various multidisciplinary rehabilitation programs?
  - d. What kinds of harms are experienced by patients participating in various multidisciplinary rehabilitation programs?
2. **Subgroups:** Does the efficacy of specific multidisciplinary rehabilitation programs vary across patient subgroups?
3. **Timing:** At what stage of recovery do multidisciplinary rehabilitation programs offer the best chance of improvement to patients?
4. **Intervention Characteristics:** Which intervention characteristics predict response in various forms of multidisciplinary rehabilitation programs?
5. **Multidisciplinary rehabilitation program versus accessible rehabilitation:** What is the comparative effectiveness of various types of multidisciplinary rehabilitation programs versus rehabilitation typically covered by third party payers?
6. **Sustainability:** Are benefits received from multidisciplinary rehabilitation programs sustained over the long-term?
7. **Followup:** What level and type of followup care allows for maintenance or prevents deterioration of rehabilitation gains at given time periods post rehabilitation?

## **Appendix B. Search Strategy for Ongoing Studies**

**Advanced search for intervention and non-intervention studies on ClinicalTrials.gov**  
‘Traumatic brain’ in the condition field

## Appendix C. Relevant Ongoing Studies

| Study ID    | Title  | Purpose  |
|-------------|--|--|
| NCT01334398 | A Health & Wellness Intervention for Individuals With Traumatic Brain Injury (TBI)   | The primary goal of the proposed study is to evaluate the efficacy of a replicable community-based group intervention, designed to address both general wellness and specific TBI health-related issues. Emphasis is placed on goal setting to develop healthy habits, utilizing problem solving strategies, learning means of maintaining progress and setting new goals. Facilitators will utilize approaches aimed at maximizing participant self-efficacy, reducing barriers to health promotion, and developing personal resources. A randomized wait-list control group design will be used to evaluate the efficacy of the intervention. It is hypothesized that individuals with TBI who participate in the intervention group will report increased health promoting behaviors, health related self-efficacy, health-related quality of life, level of participation, and greater perceived wellness and satisfaction with life as compared with the control group. |
| NCT00233129 | Improving Executive Functions After Traumatic Brain Injury (TBI): A Clinical Trial of the "Executive Plus" Program                                     | This is a randomized clinical trial which compares a standard day treatment program for individuals with TBI with the "Executive Plus" program; the latter emphasizes training of attention, emotional self-regulation and problem solving. The goal of the Executive Plus program is to maximize executive functioning, as well as the long-term outcomes of community participation and satisfaction with daily life.  |
| NCT00627237 | Improving Executive Functioning After Traumatic Brain Injury (TBI): A Trial of the "Short Term Executive Plus" Program                                 | The purpose of this study is to determine the efficacy of an intensive short term cognitive rehabilitation program aimed towards improving executive functioning in individuals with traumatic brain injury (TBI).   |
| NCT00676182 | Telerehabilitation for Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) Returnees With Combat-Related Telerehab for Traumatic Brain Injury | The scientific objective of this program is to meet the rehabilitation needs of combat wounded veterans with mild to moderate Traumatic Brain Injury (TBI) via telerehabilitation and determine the effect of this modality of care on patients' physical health and outcomes including function and community participation. We will also evaluate the benefits and limitations of rehabilitation using telehealth from the veteran and caregiver perspectives and evaluate the impact of rehabilitation via telehealth on Veterans Affairs health care facility use.   |
| NCT00704067 | Improving Work Outcomes for Veterans With Traumatic Brain Injury   | The 12-month study will investigate a cognitive training augmentation of supported employment to improve cognitive performance and work outcomes, which are expected to result in improved quality of life and community integration for veterans with mild to moderate traumatic brain injuries. The primary hypothesis is that compared with veterans who receive enhanced supported employment, those who receive supported employment plus cognitive training will work more weeks during the 12 months.   |

| <b>Study ID</b> | <b>Title</b>   | <b>Purpose</b>  |
|-----------------|--|---|
| NCT00714428     |  | <p>Development of Quality of Life Tool for TBI (TBI QOL)</p> <p>O1: Identify a parsimonious set of domains that capture HRQOL in deployment-related TBI.</p> <p>O2: Construct and refine clinically-relevant HRQOL of life item banks for deployment-related TBI, in order to</p> <p>O3: Utilize Item Response Theory methodology to refine and calibrate targeted and generic item banks for use with</p> <p>O4: Develop a short form, refining item sets and developing algorithms for future development of a computerized</p>   |
| NCT01020318     | Evaluation of Outcome Measures for Patients Diagnosed With Traumatic Brain Injury  | To evaluate potential test instruments in patients with TBI. To evaluate patient tolerance of an extensive battery of assessments and the time required to complete the assessments. To improve staff competencies on new or novel assessments of the TBI patient population  |
| NCT01132898     | Long-term Clinical Correlates of Traumatic Brain Injury  | The primary objective is to contribute to the understanding of non-penetrating traumatic brain injury (TBI) through the description of the relationships between neuroimaging, hematological, and extensive functional/cognitive phenotyping measures. We will generate natural history data for cohort-based comparisons and to serve as the basis for future hypothesis-driven protocols. In addition, we will create and test a series of new taxonomies to describe TBI severity and predict outcome.   |
| NCT01138020     | Cognitive Rehabilitation of Blast Traumatic Brain Injury (TBI)   | The purpose of this study is to investigate the efficacy of a structured rehabilitation program on cognitive function and quality of life in individuals with blast-induced traumatic brain injury (bTBI).  |
| NCT01158781     | Restoration of Life Role Participation Through Integrated Cognitive and Motor Training for Individuals With Traumatic Brain Injury (TBI) | The purpose of this study is to restore life role participation for those with TBI by customizing, applying, and testing integrated cognitive and motor training protocols that were successful in populations with impairments similar to TBI. The treatment protocols are based on principles of brain plasticity and re-learning, required to restore cognitive and motor function. The intervention targets an array of impairments that are obstacles to life role participation. These include cognitive attention and executive control; motor control for upper limb function; balance and gait; and cognitive executive control of simultaneous cognitive and motor tasks required by everyday tasks. The intervention utilizes training specificity, framing the intervention within functional task and life role activity component practice. |

| <b>Study ID</b> | <b>Title</b>   | <b>Purpose</b>  |
|-----------------|--|---|
| NCT01166386     | Acute Neurobehavioral Program for Improving Functional Status After TBI            | Our long-term goal is to lessen these burdens through improving the functional status of patients with TBI by providing an evidence-based, comprehensive, brief, acute-care intervention, First Steps Acute Neurobehavioral and Cognitive Intervention (FANCI). The 10-session, manualized FANCI Program will be tested in a controlled, randomized study.  |
| NCT01420939     | Developing Therapies for Traumatic Brain Injury                                    | To collect medical information from people with recent traumatic brain injury and compare this information to that of healthy volunteers and of persons who have had injuries to other parts of their bodies besides their heads (such as broken bones, orthopedic injuries, after surgery).  |
| NCT01565551     | Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) | Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI): The global aim of this proposal is to test and refine Common Data Elements (CDEs), neuroimaging standards, and best practices for genetics and proteomics in Traumatic Brain Injury (TBI) studies. Testing and validating of TBI-CDEs will be performed in a multi-center prospective observational study with 3 TBI Centers (San Francisco General Hospital, University of Pittsburgh Medical Center, University Medical Center Brackenridge) and a TBI Rehabilitation Center (Mount Sinai Rehabilitation Center). The investigators will create and expand existing data repositories for patient demographics, neuroimaging, plasma biomarkers, genetics, and multivariate outcomes thereby providing researchers and clinicians with the infrastructure to establish multidisciplinary, multicenter research networks and improve clinical research in the TBI field. |